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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/435,249 11/05/99 SCHNEIDER J SCH01.NP001

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CLIFFORD KENT WEBER ESQ
THOMAS JEFFERSON UNIVERSITY
OFFICE OF UNIVERSITY COUNSEL
1020 WALNUT STREET SUITE 620
PHILADELPHIA PA 19107-5587

EXAMINER

SCHMIDT, M

ART UNIT

PAPER NUMBER

1635

DATE MAILED:

01/03/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/435,249

Applicant(s)

Schneider

Examiner

Schmidt

Group Art Unit

1635

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Response

A SHORTENED STATUTORY PERIOD FOR RESPONSE IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a response be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for response specified above is less than thirty (30) days, a response within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for response is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to respond within the set or extended period for response will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

- ☒ Responsive to communication(s) filed on 9/29/00.
- ☒ This action is FINAL.
- ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- ☒ Claim(s) 1-22 is/are pending in the application.
- ☐ Of the above claim(s) is/are withdrawn from consideration.
- ☐ Claim(s) is/are allowed.
- ☒ Claim(s) 1-22 is/are rejected.
- ☐ Claim(s) is/are objected to.
- ☐ Claim(s) are subject to restriction or election requirement.

Application Papers

- ☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- ☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
- ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- ☐ The specification is objected to by the Examiner.
- ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

- ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
 - ☐ All ☐ Some ☐ None of the CERTIFIED copies of the priority documents have been received.
 - ☐ received in Application No. (Series Code/Serial Number) _____.
 - ☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

Attachment(s)

- ☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 3
- ☐ Interview Summary, PTO-413
- ☐ Notice of References Cited, PTO-892
- ☐ Notice of Informal Patent Application, PTO-152
- ☐ Notice of Draftsperson's Patent Drawing Review, PTO-948
- ☐ Other _____

Office Action Summary

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DETAILED ACTION

1. Claims 1-22 are pending in the instant application. This Official Action on the Merits is in response to the response filed 09/29/00.

Claim Rejections - 35 USC § 112

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Claims 1-22 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for administration of specific antisense oligonucleotides for therapeutic purposes claimed, does not reasonably provide enablement for administration of any such antisense or triplex therapeutic molecule for the functions claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims for the same reasons of record as set forth in the Official Action on the Merits mailed 03/30/00.

Applicant's arguments filed 09/29/00 have been fully considered but they are not persuasive.

Applicant argues that the specification as filed is fully enabling for the scope of treatment of any mammal for Parkinson's disease via administering a therapeutically effective amount of antisense oligonucleotide to the substantia nigra pars reticulata for the downregulation of glutamic acid decarboxylase as broadly claimed.

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Examiner maintains the position that the specification as filed is not enabling for the administration of any such antisense oligonucleotide via any route of administration to any mammal as broadly claimed for the reasons argued in the previous Official Action on the Merits mailed 03/30/00 and as reiterated and supported below.

In summary, Applicant addresses several key issues cited by Examiner as areas of unpredictability in the art for administration of antisense oligonucleotides to whole organisms and cites evidence in the specification for such administration and arguments which further address the legal burden of Applicant to meet the standards for enablement of Applicant's invention.

Following is a response to each of the key points argued by Applicant:

(1) On page 3 of the response, Applicant notes that "Applicant's invention relates to methods of treatment of Parkinson's disease in a mammal, wherein an oligonucleotide is delivered directly to a specific area of the brain, wherein an oligonucleotide is delivered directly to a specific area of the brain, by direct injection into that specific region of the brain, for downregulation of the specific target, wherein the target is GAD65 and/or GAD67, glutamate receptors, or GABA receptors." First, however, it is noted that the claims are broadly drawn to any route of administration of an antisense oligonucleotide. Neither the specification nor the art provide general guidelines for administration of antisense oligonucleotides to whole organisms as argued previously such that one skilled in the art would be able to make and use the scope of possible antisense oligonucleotides for the functions claimed. Applicant further notes that the specification teaches how to design antisense oligonucleotides (bottom of page 3 of the response filed

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09/29/00) and that the art provides rodent and primate models for Parkinson's disease on which to test such antisense oligonucleotides (page 4 of the response filed 09/29/00). However, as argued previously, design of antisense oligonucleotides which are functional in vivo is not an art accepted practice. The art teaches (note Branch, cited previously) that often antisense oligonucleotides which are effective in cells in culture often are not successful in cells in whole organisms depending on several factors such as accessibility of target gene, degradation of the antisense, toxic levels required to function, etc. Although whole organism models may be known in the art, neither the specification nor the art provide sufficient guidance for the design of antisense which function as broadly claimed. One skilled in the art would necessarily practice an undue amount of experimentation to design, modify and develop the antisense oligonucleotides broadly claimed for the functions claimed, treatment of Parkinson's disease in any mammal.

(2) Applicant cites decisions by the Federal Circuit to support the argument that "the administration of any oligonucleotide to the target nucleic acid will inhibit, to varying efficiencies, the expression of the target GAD65 and/or GAD67, glutamate receptors, or GABA receptor nucleic acids." (Page 4 of the response filed 09/29/00) In response, Examiner does not disagree with the above statement stating that "the administration of any oligonucleotide to the target nucleic acid will inhibit, to varying efficiencies, the expression of the target...." The rejection of the pending claims is instead drawn to the breadth of the scope of the claimed invention in view of the functions claimed: the treatment of Parkinson's disease in any mammal via administration of any antisense of the breadth claimed. Neither the specification nor the art teach guidance for the

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breadth of the scope of the claims as argued above. Thus although it would be expected that administering an antisense oligonucleotide via any route of administration to any whole organism would, to some extent, effect the expression of the target, this act alone will not allow one skilled in the art to make and use that antisense to treat a disease.

Further, Applicant cites specific examples in the art in support that administration of antisense oligonucleotides to mammals is enabled in the art for therapeutic purposes. In response, although specific examples are known in the art for therapeutic administration of antisense to whole organisms, several unpredictable factors in the art preclude the assumption that one skilled in the art would be able to correlate the success of those antisense oligonucleotides to the ones claimed in the instant application. These unpredictable factors stem from the factors argued previously: stability of the antisense in vivo, routes of administration, toxicity, etc. Applicant cites examples relating to certain situations, but does not teach how the success of such examples correlates to the instant case for treatment of a specific disease in any mammal.

Thus the rejection stands that one skilled in the art would necessarily practice "trial and error" experimentation to design and test the scope of claimed antisense oligonucleotides since the art clearly teaches the unpredictability of such methods.

In summary, the amount of experimentation one skilled in the art must accomplish to design and administer the scope of claimed oligonucleotides would require undue amount of experimentation to make and use the invention as broadly claimed.

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Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to *Mary M. Schmidt*, whose telephone number is (703) 308-4471.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *George Elliott, Ph.D.* may be reached at (703) 308-4003. The examiner's primary, *John LeGuyader*, may be reached at (703) 308-0447.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group Analyst, *Katrina Turner*, whose telephone number is (703) 305-3413.

M. M. Schmidt
January 1, 2001



REMY YUCEL, PH.D
PRIMARY EXAMINER